REMARKS

Claims 1, 7, 9-11, 14-86, 88-90, 93, 95-105, 107-117, and 119-145 are pending in the present application. Claims 14-84, 96, 107-109, 111-117, and 119-121 were previously withdrawn from consideration and claims 2-6, 8, 12-13, 87, 91, 92, 94, 106, and 118 were previously cancelled. In this response, claims 1, 85, 86, 122-127, 132, 134-139, and 144 have been have been amended, and claims 128 and 140 cancelled. Support for the claim amendments is found, among other places, in paragraphs [0099], [0103], [0109] and [0171], and in Table 1 on page 72 of the specification as originally filed. No new matter is added. Accordingly, claims 1, 7, 9-11, 85-86, 88-90, 93, 95, 97-105, 110, 122-127, 129-139, and 141-145 remain under consideration. Amendment and cancellation of certain claims is not to be construed as a dedication to the public of any of the subject matter of the claims as previously presented.

Claim Rejections – 35 USC §112

Claims 132 and 144 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. The Office states that the recitation of "at least six months" effectively claims no upper limit to the duration of pain relief, and that the specification does not support such an unlimited upper limit.

Claims 132 and 144 have been amended to recite that a single application of the liquid formulation results in pain relief for up to about six months. Applicants submit that this amendment renders the rejection moot.

Accordingly, withdrawal of the rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

Claim Rejections – 35 USC §103

Claims 1, 7, 9, 10, 11, 85, 86, 88-90, 93, 95, 97-105, and 122-145 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over the combined disclosures of O'Neill et al. (EP 0 347 000) ("O'Neill") in view of LaHann et al. (U.S. 4,546,112) ("LaHann"), and in further

view of Beerse et al. (U.S. 5,968,539) ("Beerse"). The Office asserts that O'Neill discloses the penetration enhancers of the claimed formulation. For example, the Office cites page 11, lines 35-41 for its description of propylene glycol, ethanol, isopropanol, and mixtures thereof as penetration enhancers, and page 10, lines 18-20 as teaching solvents that include fatty acid esters and alcohols such as oleyl alcohol. Although O'Neill is silent with respect to the claimed TRPV1 agonist concentrations above 5%, the Office further states that it would have been obvious to one of ordinary skill in the art to apply higher concentrations in view of LaHann, which discloses a formulation purportedly including 1-25% capsaicin, in order to provide a reduction in irritation to the end user and to optimize the dosage.

The Office also asserts that a compound and its properties cannot be separated. Thus, the practice of applying a formulation of the prior art comprising the same components of the instant claims will inherently provide pain relief for up to six months.

Applicants strongly disagree with this rejection. Claims 1, 85, and 86 have been amended to include a list of specific first and second penetration enhancers. Obviousness (and inherency) has not been established at least because the cited references, alone or in combination, lack disclosure of the claimed penetration enhancers. The Office is respectfully reminded that independent claims 1, 85, and 86 recite liquid formulations having at least a first and a second penetration enhancer, where the first and second penetration enhancers are separately selected from the group consisting of propylene glycol, diethylene glycol monoethyl ether, ethyl oleate, oleic acid, and oleyl alcohol, benzyl alcohol, and menthone.

O'Neill fails to disclose first and second penetration enhancers as claimed. First, it is important to note, that O'Neill separates out various delivery forms (e.g., lotions, creams, solutions, gels, solids, etc.) and then describes each of those in more detail. With respect to "solutions," which in view of the liquid formulations recited by Applicants' instant claims is the only possibly relevant form O'Neill describes, O'Neill states that propylene glycol, polyethylene glycol (M.W. 200-600), polypropylene glycol (M.W. 425-2025), glycerine, sorbitol esters, 1,2,6-hexanetriol, ethanol, isopropanol, diethyl tartrate, butanediol, and mixtures thereof are useful (page 11, lines 8-10). As

can be seen, no combination of O'Neil's penetration enhancers results in Applicants' claimed combination. Neither LaHann nor Beerse cure this deficiency.

Applicants further note that O'Neill also fails to disclose the claimed amount of TRPV1 agonist. Applicants have amended independent claims 1, 85, and 86 to recite that the liquid formulation comprises between about 6% (w/v) to about 60% (w/v) of the TRPV1 agonist. O'Neill teaches that an effective amount of a vanilloid compound (e.g., a TRPV1 agonist) is from 0.001% to 5% in all of the disclosed forms, i.e., lotions, creams, solutions, gels, and solids (*see, e.g.*, page 9,line 29; page 10, line 56; and page 11, lines 6, 24, and 32). Higher concentrations of TRPV1 agonist are nowhere taught, disclosed, or even suggested. Indeed, the Office concedes that O'Neill fails to disclose concentrations above 5% (w/v) (*see, e.g.*, the first full paragraph on page 4 of the instant Office Action).

Accordingly, LaHann is used by the Office to provide support for the claimed higher concentration of TRPV1 agonist. However, LaHann clearly teaches away from using high concentrations of capsaicin. Indeed, LaHann discourages the use of capsaicin concentrations above about 2% (*see, e.g.,* column 3, lines 12-19), stating that "high concentrations, e.g., above about 2%, of capsaicin and/or its salt(s) can cause reddening of the skin, as well as a burning sensation..." Moreover, contrary to the Office's assertion, the single highest concentration of capsaicin mentioned in the cited reference is 8% capsaicin (Example 3), not 25% capsaicin. The 1%-25% stated at column 3, lines 34-40 (relied upon by the Office) is clearly referring to the concentration of the emollient, not capsaicin. However, regardless of the concentration of capsaicin disclosed by LaHann, Applicants reiterate that because LaHann does not cure the deficiency of O'Neill with respect to the penetration enhancer combinations, it cannot be said that O'Neill in view of LaHann renders the instant claims obvious.

Applicants also reiterate that all independent claims require that a single application of the liquid formulation results in pain relief for at least about two weeks. None of the references disclose this limitation, and because none of the references disclose Applicants' formulation, it cannot be said that this limitation is merely an inherent result of a prior formulation.

Applicants further note that the combination of LaHann and O'Neill does not render the instant claims obvious because one of skill would not even look to combine O'Neill with LaHann. Indeed, if the Office maintains that LaHann is useful for its disclosure of high concentrations of capsaicin, Applicants note that O'Neill at page 11, lines 51-55, clearly defines and puts limits on what a "safe and effective amount" of a compound would be. Indeed, O'Neill states that the phrase "safe and effective amount" as used in the application, "means an amount of a compound or composition high enough to significantly positively modify the condition to be treated, but low enough to avoid serious side effects..." When O'Neill describes solutions (paragraph 3, pg. 11) he states that an effective amount of a vanilloid compound is from "0.001% to 5%, more preferably from 0.1% to 1%." That is, O'Neill throughout his disclosure suggests that amounts above 5% of a vanilloid are not safe, and clearly prefers low concentrations (i.e., 0.1-1%) of them. Therefore, even if LaHann were useful for support of high concentrations of capsaicin (which Applicants do not concede), there is no logical rationale an ordinary artisan would look to combine LaHann with O'Neill for that purpose.

With O'Neill and LaHann removed as references, Beerse, which describes rinse-off compositions, cannot be used to further establish a case of obviousness.

At least in view of the above, withdrawal of the rejection under 35 U.S.C. §103(a) is respectfully requested.

Double Patenting

Claims 85, 86, 88-90, 93, 95, and 97-103 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1, 16, 17, 20, 21, 24, 25, 28, 39-45, 47, 50-54, and 60-63 of co-pending Application No. 11/411,328. Applicant will consider filing a terminal disclaimer after receiving an indication that each of the currently rejected claims is allowable. Until then, Applicant has no real way of assessing the merits of the double patenting rejection or determining whether the filing of a terminal disclaimer is appropriate.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 524522001300. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

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